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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/884,873	06/30/97	COOK	ISIS-2202

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HM21/0508

EXAMINER

RICIGLIANO, J

ART UNIT PAPER NUMBER

1648

DATE MAILED: 05/08/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary

Application No.
08/884,873

Applicant(s)
Cook, Phillip Dan

Examiner
Jos ph W. Ricigliano Ph. D.

Group Art Unit
1648



☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-30 is/are pending in the applicat

Of the above, claim(s) 27-30 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-26 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-27, drawn to mixtures of purine and pyrimidine compounds, classified respectively in class 544 subclass 264 and class 544, subclass 242.
 - II. Claims 27-30, drawn to a method of preparing a combinatorial library, classified in class 435, subclass 7.1.
2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the products as claimed can be made by materially different process such as cyclization reactions rather than reactions starting with a heterocyclic scaffold.
3. During a telephone conversation with John W. Caldwell on 4/28/98 a provisional election was made without traverse to prosecute the invention of group I, claims 1-26. Affirmation of this election must be made by applicant in replying to this Office action. Claims 27-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

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Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for activity against fungus mold mildew, does not reasonably provide enablement for a form of decay. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

6. Claim 25 recites the phrase “form of decay” in reference to the activity of mixtures of purine and pyrimidines. The scope of “form of decay” includes ageing, the rusting out of a boat’s hull and the loss of soil from a stream bank. Applicants have not taught how to make or use mixtures of purines or pyrimidines that have activity against forms of decay such as aging, hull rusting, or the loss of soil from a stream bank. Considering the high level of unpredictability in the art, in the absence of guidance by the applicant it would require undue experimentation for one of skill in the art to make and use a product commensurate with the scope of the claimed invention.

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7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 7, 9, 11, 12, 14, 15-19 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 9 are directed to scaffolds or tethers that have an atom that is nucleophilic. This is indefinite because it is unclear under what conditions the atom is to be nucleophilic. Therefore, it is not possible to clearly define the metes and bounds of the claimed invention.

Claims 11 and 12 are directed to substituents that are electrophilic. This is indefinite because it is unclear under what conditions the substituents are to be electrophilic. Therefore, it is not possible to clearly define the metes and bounds of the claimed invention.

Claims 14 and 15 recite the phrase "synthesized simultaneously in solution." This is vague and indefinite because it is unclear if it is intended to mean the entire set of synthetic reactions is conducted in one step or if the applicant intends the phrase to mean the mixture is synthesized together in solution although multiple steps are required.

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Claims 14 and 15 recite the phrase "solution phase." This is vague and indefinite because it is unclear what limitations apply to "solution phase." For example, syntheses conducted on soluble polymeric supports considered to be in the solution phase or are only reactions conducted without any support matrices considered to be in the solution phase? Therefore, it is not possible to clearly define the metes and bounds of the invention as claimed.

Claim 16 recites the limitation "said process" in claim 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 is directed to product, which is a mixture, and does not recite a process.

Claims 17 and 18 recite the use of a further reactant to modify components of the mixture. This is indefinite because it is not possible to determine what limitations apply to a reaction employing an unspecified reactant, which may be comprised of an unspecified number of reagents to undertake an unspecified type of reaction and which produces an unspecified product. Therefore it is not possible to determine or clearly define the metes and bounds of the invention as claimed.

Claim 19 recites "wherein the heterocyclic portion of said chemical compounds are ring-opened, ring expanded, bicyclized, or altered in subsequent to said substitution at said at least one of said functionalizable atoms." This is indefinite because upon ring-opening, ring expansion, bicyclization, or alteration subsequent to the substitution at one functionalizable atoms by unstated processes with unspecified reagents it is not possible to clearly define the structure of the

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products. Therefore it is not possible to clearly define the metes and bounds of the claimed invention.

Claim 19 recites the phrase "ring closed" in relation to the purine or pyrimidine heterocyclic scaffolds. Since these scaffolds are already ring structures, the concept of closing a ring in the heterocycle portion of these structures is vague and indefinite. For example it is unclear if applicant intends to close a new ring bridging the purine scaffold or if applicant intends to close the 5 member ring of a purine to produce a pyrimidine. Therefore, it is not possible to clearly define the metes and bound of the claimed invention.

Claim 25 recites a "form of decay." This is indefinite because it is unclear what limitations apply to "decay." Therefore, it is not possible to define the metes and bounds of the invention as claimed.

Claim 25 recites mixtures having activity against: agricultural pests or house hold pests. These terms are indefinite because it is unclear what constitutes a household pest or an agricultural pest and what limitations apply to a household pest or an agricultural pest. Therefore, it is not possible to clearly define the metes and bound of the claimed invention.

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Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 3, 5 and 13-15 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Michnick et al [US 5,470,878].

Michnick et al. teach a pharmaceutical composition “comprised of one or a plurality of inventive compounds,” (col 22 lines 32-38), which reads on a mixture. Michnick et al teach more than thirty different N-1-substituted 3,7-dimethyl xanthine derivatives (not counting the R and S derivatives separately; see column 24 line 24-26 and the structures starting at compound #27 in column 34 to compound 74) this reads on mixtures of 15 or more compounds substituted with at least 6 different chemical substituents having a common purine scaffold and at least two functionalizable atoms, said scaffold having substitution on at least one functionalizable atom. The xanthine scaffold has at least three functionalizable atoms (nitrogens 1, 3 and 7), which reads on the specific limitation of claim 5. The methyl groups on nitrogens 3 and 7 serve to block a functionalizable atom, the specific limitation of claim 13. Therefore Michnick et al clearly anticipates the mixtures of claims 1, 2, 3, 5 and 13-15.

10. Claims 1-15 and 20-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Summerton et al [5,506,337].

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Summerton et al teach the formation of morpholino subunit libraries. These libraries having substituted purine or pyrimidine heterocycles present (see figs 5a and 5b) which read on the purine or pyrimidine heterocyclic scaffold of the instant invention. Summerton et al. teach that the purine and pyrimidines can be substituted with a wide variety of substituents including aliphatic groups at multiple sites on the scaffold, which reads on the six different substituents and three or more functionalizable atoms, as required in claim 5 of the instant application (R1, R2, R3 and X; see figure 5 and its legend starting col 8 line 26). The morpholino subunit which attaches the purine or pyrimidine nucleotides to other bases reads on a tether with at least one functionalizable atom substituted with a chemical substituent (a limitation of claims 8, 10 and 23) or alternatively, a substituent on the pyrimidine or purine scaffold. The other morpholino bases in the oligomers of Summerton et al read on different chemical substituents. Any mixture of these which employs the same purine or pyrimidine scaffold with more than six substituents reads on the mixtures of the instant application. Summerton et al teach the libraries preferably contain 10^4 to 10^7 different sequences, which reads on the limitation of claims 2, 3, 21 and 22 (col 11 lines 43-56). Summerton et al teach that roughly equimolar mixtures of oligomers can be made by adjusting the concentration of each subunit which reads on the limitation of claim 4 (compounds are within 20 mole percent of equimolarity in the mixture). The purine or pyrimidine scaffolds contain nitrogen atoms which read on nucleophilic atoms in the scaffolds, a specific limitation of claims 7. The morpholino group contains a nitrogen which reads on a functionalizable group of the tether being nucleophilic, a specific limitation of claim 9. Summerton et al teach that esters

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can be a substituent on the morpholino groups (figure 5C compound number 5 where X is OR) this reads on an electrophile since the group present would be subject to nucleophilic attack (Michael addition). Summerton et al teach the substituent on the purine or pyrimidine ring can be aliphatic, which includes linear alkenes and alkynes which can serve as electrophiles (col 8 line 37), a limitation of claim 12. The aliphatic substituents can also function to chemically block a functionalizable atom of the scaffold, the specific limitation of claim 13. Summerton et al teach that the use of iterative synthesis to create the molecules of the mixtures, a limitation of claim 15 (synthesis requiring repeated cycles of applying groups, removing protecting groups etc., see figure 13). Summerton et al teach that the compounds of their invention can be synthesized on solid supports or in solution, a limitation of claim 14 (Col 12 lines 3-8 and col 17 starting line 25). Therefore, Summerton et al anticipates the mixtures of claims 1-15 and 18-26.

11. Claims 1-3, 5-15, and 17-26 are rejected under 35 U.S.C.102(b) as being anticipated by Pavia et al.

Pavia et al teach a structurally diverse universal library. Pavia et al teach that their libraries are composed of scaffold molecules and at least three functional groups (page 4 line 26) which reads on a scaffold having at least three functionalizable atoms and being substituted at two or more positions. Pavia et al teach that "more preferred" scaffold groups include a pyrimidine rings (page 7 line 21-23) which reads on one of the heterocyclic scaffolds recited in claim 1 in the alternative. Pavia et al teach that the libraries of their invention can be prepared on a solid phase

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or in solution, (page 17) which reads on a mixture. The libraries prepared by Pavia et al can be synthesized by combinatorial methods and contain more than one million compounds, which reads on libraries containing least 6, 10 or 15 compounds (page 16). Pavia et al also teach the use of more than six chemical substituents to substitute the scaffold (see R and W groups on page 6) and the tether groups connecting the chemical substituents to the scaffold (see the A, M or M-bound to a second ring on page 6) which reads on at least six different chemical substituents and the tether groups of the instant invention. On pages 5-7 Pavia et al teach that their tethers and scaffolds include nitrogen substituted nitrogen (NR_{60} , which reads on a functionalizable tether atom which is nucleophilic, substituted and on the scaffold; see the limitations of claims 7-10); S (which reads on a nucleophile) and alkenes (which reads on an electrophile). Pavia et al teach other substituents that can be electrophilic or nucleophilic on their scaffolds; for example a Br-substituted alkane has an electrophilic carbon and the -SH moiety reads on a nucleophile. As noted above, Pavia et al teach adding substituents to functionalizable atoms (for example the addition of a W group, see pages 5-7), which reads on blocking the functionalizable atoms, a specific limitation of claim 13. Pavia also teaches deprotecting mixtures (see scheme Va, page 36 for example), which reads on reacting mixtures with a further reactant. Pavia teaches the addition of a second (and a third) set of substituents to an already formed mixture which reads on reacting a mixture with a further reactant at the heterocyclic portion and altering subsequent to substitution, limitations of claims 18 and 19 (see scheme I-III page 21 and pages 5-7). Therefore, Pavia et al teach the invention of claims 1-3 and 5-15 and 17-26.

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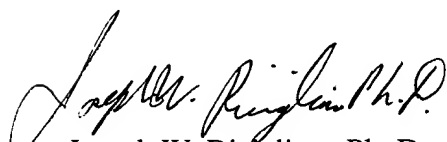
12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kim et al Dendrimer-Supported combinatorial chemistry. Proceedings of the National Academy of Science (USA)93:10012-10017 (1996). Kim et al teach the use of supports in for combinatorial synthesis which allow the synthesis to be conducted in solution, there by forming libraries or mixtures in solution.

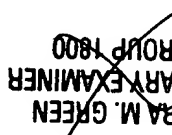
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph W. Ricigliano Ph. D. whose telephone number is (703) 308-9346. The examiner can normally be reached on Monday through Thursday from 7:30 A.M. to 5:00 P.M. and alternate Fridays from 7:30 A.M. to 5:00 P.M.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald Adams, can be reached at (703) 308-0570.



Joseph W. Ricigliano Ph. D.


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